production, transcription, translation or activity of 14 kDa PLA_2 and wherein the compounds were invented after the priority date of March 26, 1996.

9. A method of treating a chronic disease of atherosclerosis in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis with an effective amount of a compound which inhibits which inhibits the production, transcription, translation or activity of 14 kDa PLA_2 and wherein the compounds were invented after the priority date of March 26, 1996.

10. The method according to claim 5 wherein the disease is diabetic retinopathy or other ocular neovascularizations.

11. The method according to claim 5 wherein the disease is tumor growth and metastasis.

12. The method according to claim 5 wherein the disease is atherosclerosis.

13. A method of treating a chronic disease in a mammal in need thereof, which disease is characterized by excessive, undesired or inappropriate angiogenesis, with an effective amount of a compound which inhibits the production, transcription, translation or activity of 14 kDa PLA_2 other than those compounds disclosed before March 26, 1996.

REMARKS

Claims 1 to 13 are in the application. Claim 5 has been amended to be an independent claim as suggested by the Examiner. Newly added claims 10 to 13 being dependent thereon. Claims 7 to 9 are also newly added, support for all of the claims residing in the original filed claims. Claims 1, 7, 8 and 9 have incorporated a proviso of sorts to remove any potential for inherency in compounds having the newly determined activity prior to Applicants filing date. No new matter is believed added.

Applicants thank the Examiner for notice of allowable subject matter.

Rejection under 35 USC §112, first paragraph

Claims 1 to 4 are rejected under 35 USC §112, first paragraph as being non-enabling to the "mechanism of Claim 1 ...claimed therein". Applicants respectfully traverse this rejection.

The Examiner indicates that the specification is enabling to treat the disorders of Claims 2 to 5 using the compounds of Formula (I) (as claimed in claim 5). However, the specification is stated to be non-enabling for "any skilled person in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The compound administered to treat inflammation as taught by

applicants at page 3 of the specification would inherently inhibit the mechanism claimed in claims 1-6".

Applicants clearly define the invention to be use of a compound which inhibits the production, transcription, translation or activity of 14 kDa PLA_2. There are many well known methods in the art to determine whether a compound inhibits this enzyme and not to be confused with the activity of another enzyme. The specification provides information on how to test for such compounds and refers to suitable US patents containing such assays (page 4, lines 16 to 22).

A suitable angiogenic model is described in the specification on page 12, lines 11 to 14, which model is also a well known model. To demonstrate the effectiveness of an inhibitor of 14 kDa PLA_2, Compound I, (the compound of claim 6) was tested in this well known model.

It is Applicants determination that PLA_2 inhibitors would be useful to treat chronic diseases associated with excessive or inappropriate angiogenesis (proliferation of blood vessels).

A compound which is used to treat inflammation would not necessarily inhibit the production , transcription, translation or activity of the 14 kDa PLA2 enzyme. However, to avoid any ambiguity in this matter, Applicants have amended Claim 1 to provide for compounds which inhibit, etc. this activity from the filing date of the priority application.

In view of these comments and amendments, reconsideration and allowance of Claims 1 to 4 is respectfully requested.

Rejection under 35 USC §103

Claims 1 to 4 are rejected under 35 USC §103 being unpatentable over Clark (US Patent 5,679,666), Beal III et al. (US 3,984,455) and Folkman et al., (US 5,001,116). Applicants respectfully traverse this rejection.

Applicants have amended the claims to remove any possibility of "inherency" by the compounds disclosed in the Clark, Beal and Folkman et al. patents by insertion of a priority date filing into the main claim

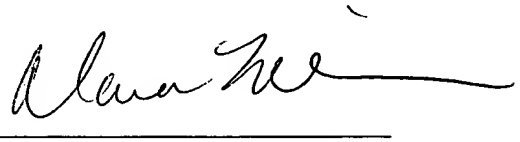
None of these references disclose or suggest inhibition of the production, transcription, translation or activity of the 14 kDa PLA2 enzyme. None of these compounds disclose or suggest that such inhibition of the production, transcription, translation or activity of the 14 kDa PLA2 enzyme would be useful to treat a disease which is characterized by excessive, undesired or inappropriate angiogenesis.

In particular, heparin is known NOT to be an inhibitor of PLA_2. The anti-angiogeneic effects of the steroids are also not known to be related to PLA_2 inhibitory activity. The literature is quite clear that the angiostatic steroids can be separated from the classical steroids structurally, but their mechanism of action in angiogenesis is not known.

In light of these remarks and amendments, reconsideration of the rejection to the claims under 35 USC §103 is respectfully requested.

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. If any additional fees or charges are required by this paper the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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